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Prevalence of chronic kidney disease and anemia among participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Cohort Study: Baseline results

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The incidence of end-stage renal disease (ESRD) is increasing in the United States population [1]. Despite the marked increased risk of ESRD among blacks in the United States population, population-based estimates show a comparable prevalence of chronic kidney disease, defined as an estimated glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2, among different ethnic groups within the United States population [2–5]. Among nondiabetic participants in the Third National Health and Nutrition Examination Survey (NHANES III), chronic kidney disease was present in 9.2% of white males, 17.8% of white females, 4.2% of black males, and 6.2% of black females [3].

Anemia is frequently associated with chronic kidney disease, and when present, serves as an independent risk factor for cardiovascular morbidity and mortality. Abramson et al [2] reported that chronic kidney disease and anemia (hemoglobin <12 g/dL in women and <13 g/dL in men) were independent risk factors for stroke in a middle-aged community-based population in the Atherosclerosis Risk in the Community (ARIC) Study, with a relative risk of 7.49 in those subjects who are anemic and had creatinine clearance <60 mL/min compared to the nonanemic participants with creatinine clearances >60 mL/min. Similarly, the combination of anemia and chronic kidney disease has a significant impact on survival after acute myocardial infarction in a study of Medicare recipients in Georgia [6].

The Reasons for Geographic and Racial Differences in Stroke (REGARDS) incidence and mortality study is a population-based cohort study of a representative sample of participants aged 45 years old and older [7]. The REGARDS Study is designed to identify factors that contribute to the excess stroke mortality among blacks and in the Southeastern United States. The purpose of this report is to describe the prevalence of chronic kidney disease and anemia, using data collected as an ancillary study of the REGARDS Study [7], and to compare the prevalence of chronic kidney disease with previous descriptions of the NHANES III participants [3].

METHODS

Subjects

The REGARDS Study cohort is being recruited from a stratified random probability sample with 20% of participants chosen from the coastal plain of North Carolina, South Carolina, and Georgia (the buckle of the Southeastern stroke belt), 30% from the remainder of North Carolina, South Carolina, and Georgia, and Tennessee, Mississippi, Alabama, Louisiana, and Arkansas, (the stroke belt), and 50% from the rest of the continental United States. Cohort selection was designed so that one half will be African American and one half white, and one half male and one half female.

Inclusion criteria

Individuals aged 45 years old and older were eligible for inclusion in the REGARDS cohort, for which enrollment began in February 2003. Beginning on May 10, 2004, the additional measures to assess anemia and renal function were added to the protocol and data from

then until March 1, 2005 are included in this report. This "Renal REGARDS" includes additional measurements of hemoglobin, serum urea nitrogen, and serum albumin, obtained at the time of the initial home visit, and excludes 8400 participants recruited to the initial REGARDS cohort before May 10, 2004. Since a total of 30,000 participants will ultimately be recruited to the REGARDS cohort, the Renal REGARDS will ultimately include approximately 24,000 participants.

Exclusion criteria

Exclusion criteria for REGARDS participation include active treatment for cancer; any serious medical condition which would prevent long-term participation; cognitive impairment as judged by the interviewer; living in a nursing home or on the waiting list for a nursing home; and a language barrier (speaks other than English). Patients with ESRD were excluded from the present analysis ($N = 28$) and participants for whom the required elements needed for the GFR estimates were missing ($N = 467$) were also excluded, leaving 6807 available for this initial assessment.

Data

Data were obtained from each participant in a multistep fashion. The participant was first contacted by a mailing followed by a telephone contact where verbal informed consent was obtained. A trained interviewer then conducted a computer-assisted telephone interview (CATI) to obtain a description of demographic factors, medical history, cognitive screening, and depression measures. Subsequently, arrangements were made for an in-home evaluation by a nurse or health-professional. During the in-home examination, written informed consent was obtained, blood pressure, height and weight and anthropometric measurements, urine and blood specimens were obtained, an electrocardiogram was performed, and a medication history collected.

The blood and urine samples were analyzed at a central laboratory for serum creatinine and blood glucose, C-reactive protein, lipid assays, and with aliquots were archived for future studies. In addition, the Renal REGARDS participants had measurements of hemoglobin, serum urea nitrogen, and albumin performed. We defined subjects as being diabetic if their fasting glucose was greater than 126 mg/dL, their nonfasting glucose was greater than 200 mg/dL, or they self-reported current treatment for diabetes.

We estimated the GFR (mL/min/1.73 m^2) using the six-variable Modification of Diet in Renal Disease study (MDRD) equation [8]:

$$\begin{aligned}\text{Estimated GFR} = 170 \\ \times[\text{serum creatinine (mg/day)}]^{-0.999} \\ \times(\text{age})^{-0.176} \times (0.762 \text{ if female}) \\ \times(1.18 \text{ if African American}) \\ \times[\text{serum urea nitrogen (mg/dL)}]^{-0.170} \\ \times[\text{serum albumin (g/dL)}]^{+0.318}\end{aligned}$$

Statistical analysis

We used descriptive analyses, including means and proportions. The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative's (NKD/KDOQI) definition of chronic kidney disease is persistent change (>90 days) in GFR [9], but only single determinations of creatinine, serum urea nitrogen, and albumin were available for the Renal REGARDS participants. Nevertheless, for these analyses, we defined chronic kidney disease as estimated GFR < 60 mL/min/1.73 m^2, using the single determination of blood parameters and the six-variable MDRD equation [8].

RESULTS

There were 6807 participants in the Renal REGARDS population through March 1, 2005, who were not on dialysis, and who were not missing any of the required elements for estimated GFR determination. The Renal REGARDS participants' mean (SD) age was 65.5 ± 9.3 (SD) years, and 88% of the participants were in their sixth to eighth decade of life. Of the 6807 participants, 4053 (60%) were white and 2925 participants (43%) were male (Table 1).

Chronic kidney disease, defined as estimated GFR < 60 mL/min/1.73 m^2, was present in 1081 (16%) of the participants (Table 1). The prevalence of chronic kidney disease increased with increasing age; nine of 316 (3%) participants, 40 to 49 years old, had chronic kidney disease; 122 of 1738 (7%) participants, 50 to 59 years old, had chronic kidney disease; 366 of 2630 (14%) participants, 60 to 69 years old, had chronic kidney disease; 399 of 1653 (24%) participants, 70 to 79 years old, had chronic kidney disease; and 185 of 470 (39%) participants aged 80 years and older had chronic kidney disease.

The prevalence of anemia was greater in participants with chronic kidney disease at all age, ethnic, and gender strata (Table 1); the average (SD) hemoglobin for participants with chronic kidney disease was 13.0 g/dL (1.6), and 13.9 g/dL (1.4) for those who did not have chronic kidney disease. There was no discernible association of age with measured hemoglobin in the participants without chronic kidney disease, but in those with chronic kidney disease,

Table 1. Characteristics of the Renal Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study participants

	Number (%)	Number (%) with chronic kidney disease[a]	Number (%) without chronic kidney disease	Average hemoglobin[b] in chronic kidney diease mean (SD)	Average hemoglobin[b] without chronic kidney diease mean (SD)
Total	6807	1081 (16)	5726 (84)	13.0 (1.6)	13.9 (1.4)
Age strata					
40–49 years	316 (5)	9 (3)	307 (97)	13.6 (0.8)	13.9 (1.6)
50–59 years	1738 (26)	122 (7)	1616 (93)	13.1 (1.7)	13.9 (1.4)
60–69 years	2630 (39)	366 (14)	2264 (86)	13.0 (1.6)	14.0 (1.4)
70–79 years	1653 (24)	399 (24)	1254 (76)	13.1 (1.6)	13.8 (1.4)
≥80 years	470 (7)	185 (39)	285 (61)	12.9 (1.3)	13.6 (1.5)
Race					
White	4053 (60)	687 (17)	3366 (83)	13.4 (1.5)	14.3 (1.3)
Black	2754 (40)	394 (14)	2360 (86)	12.4 (1.6)	13.4 (1.4)
Gender					
Male	2925 (43)	384 (13)	2541 (87)	13.7 (1.7)	14.6 (1.3)
Female	3882 (57)	697 (18)	3185 (82)	12.7 (1.4)	13.3 (1.2)

[a]Chronic kidney disease defined as estimated glomerular filtration rate (GFR) <60 mL/min/1.73 m^2.
[b]Average hemoglobin (g/dL) ± SD.

Table 2. Chronic kidney disease prevalence in nondiabetic Renal Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study and the Third National Health and Nutrition Examination Survey (NHANES III) participants by age strata

	Renal REGARDS				NHANES III[a]			
	Number (% of the relevant age, gender, and ethnic group) (95% CI)				Number (% of the relevant age, gender, and ethnic group) (95% CI)			
	White		Black		White		Black	
Age Strata	Males ($N = 1548$)	Females ($N = 1898$)	Males ($N = 718$)	Females ($N = 1250$)	Males ($N = 2729$)	Females ($N = 2882$)	Males ($N = 845$)	Females ($N = 729$)
All	176 (11.4) (9.8, 13.0)	345 (18.2) (16.5, 19.9)	62 (8.6) (6.5, 10.7)	157 (12.6) (10.8, 14.4)	721 (26.4) (24.7, 28.1)	1085 (37.6) (35.8, 39.4)	101 (12.0) (9.8, 14.2)	145 (15.6) (13.0, 18.2)
40–49 years	1 (1.4) (0, 4.1)	2 (2.4) (0, 5.7)	2 (4.4) (0, 10.3)	2 (2.8) (0, 6.6)	26 (3.7) (2.3, 5.1)	88 (12.1) (9.7, 14.5)	4 (1.4) (1.0, 2.7)	9 (2.2) (0.7, 3.7)
50–59 years	12 (3.7) (1.7, 5.7)	34 (6.5) (4.4, 8.6)	9 (4.2) (1.5, 6.9)	18 (5.1) (2.8, 7.4)	66 (13.5) (10.5, 16.5)	130 (22.9) (19.4, 26.4)	10 (6.0) (2.3, 9.7)	14 (7.1) (3.6, 10.6)
60–69 years	48 (8.1) (5.9, 10.3)	128 (17.6) (14.8, 20.4)	23 (8.9) (5.5, 12.3)	57 (12.0) (9.1, 14.9)	179 (27.2) (23.8, 30.6)	246 (40.0) (36.1, 43.9)	36 (17.1) (12.0, 22.2)	56 (29.7) (23.2, 36.2)
70–79 years	76 (18.1) (14.4, 21.8)	123 (28.2) (24.0, 32.4)	16 (10.5) (5.6, 15.4)	56 (20.0) (15.3, 24.7)	199 (42.4) (37.9, 46.9)	307 (56.9) (52.7, 61.1)	40 (31.5) (23.5, 39.5)	38 (36.6) (27.3, 45.9)
≥80 years	39 (29.1) (21.4, 36.8)	58 (45.3) (36.7, 53.9)	12 (27.9) (14.5, 41.3)	24 (32.9) (22.1, 43.7)	251 (62.1) (57.4, 66.8)	314 (72.1) (67.9, 76.3)	11 (35.0) (18.5, 51.5)	28 (63.3) (48.9, 77.4)

[a]Data extracted from Figure 1 in reference [3].

there was a trend for lower average hemoglobin levels with increasing age (Table 1).

Of the 6807 Renal REGARDS participants, 1395 (20%) had diabetes. Chronic kidney disease was more prevalent among the diabetic participants (341 of 1395) (24.4%) than nondiabetic (749 of 5412) (13.7%). The prevalence of chronic kidney disease in the nondiabetic participants is shown in Table 2 by age strata, race, and gender, with 95% CIs for the proportions. Chronic kidney disease was present in 11.4% of white males, 18.2% of white females, 8.6% of black males, and 12.6% of black females. The prevalence of chronic kidney disease increased progressively with age in each of the gender and ethnic strata, and the prevalence of chronic kidney disease in females generally exceed that in males, especially in participants 60 years or older.

DISCUSSION

The United States Renal Data System has documented persistent excess among blacks in the age-gender adjusted incidence and point prevalence ESRD rates. In 2002, the ESRD incidence rates were 982 and 256 persons per million, among blacks and whites, respectively, a 3.8-fold excess risk of ESRD for blacks [1]. Rates for cause-specific ESRD, including disease attributable to hypertension and diabetes (which account for over 70% of incident ESRD in the United States) show similar racial disparities [1]. Examination of large cohorts of participants, like REGARDS and NHANES III can provide population estimates of the prevalence of chronic kidney disease, with the implication being that the incidence of ESRD is driven by the chronic kidney disease prevalence.

The overall prevalence of chronic kidney disease in the currently recruited Renal REGARDS cohort is approximately 16%, (Table 1). There was a slight excess of chronic kidney disease in white compared to black participants (17% versus 14%), and in the females compared to the males (18% versus 13%) (Table 1). The prevalence of chronic kidney disease (based on a single creatinine, serum urea nitrogen, and serum albumin measurement) increased with the age strata of the Renal REGARDS participants (Table 1). There were no major associations of gender and ethnicity with average hemoglobin. The expected relationship between chronic kidney disease and hemoglobin was observed, with the average hemoglobin (SD) of 13.0 (1.6) g/dL in the participants with chronic kidney disease and 13.9 (1.4) g/dL in the non-chronic kidney disease Renal REGARDS participants. It is not surprising that chronic kidney disease was more prevalent among diabetic participants (24.4%), than among nondiabetic participants (13.7%).

Our observations for the current nondiabetic Renal REGARDS participants are compared to the chronic kidney disease prevalence reported for nondiabetic participants from the NHANES III study in Table 2. Clase, Garg, and Kiberd [3] reported that the prevalence of chronic kidney disease in an analysis of NHANES III; among adults aged 20 years and older, 9.2% for white men; 17.8% for white women; 9.2% for black men; and 6.3% for black women. When their analysis was limited to nondiabetic whites and blacks, and subjects aged 40 years and older, the observed prevalence of chronic kidney disease was 26.4% for white males, 37.6% for white females, 12.0% for black males, and 15.6% for black females (Table 2). As is also seen in Table 2, the prevalence of chronic kidney disease in the Renal REGARDS participants was much lower at almost all ages. When the gender and ethnic strata were compared with their 95% CIs, the prevalence for chronic kidney disease in the white Renal REGARDS participants are less than half of the NHANES III results, and these 95% CIs do not overlap. The same pattern is seen comparing the black participants in the two studies, but the 95% CIs overlap. The study design and recruitment strategy were not the same for the two studies; specifically, the recruitment strategy for REGARDS included adults 45 years of age or older, with equal representation of blacks and whites, males and females, and a broad geographic base. The recruitment strategy for NHANES III included younger participants than the REGARDS study. Our preliminary analysis suggests that the prevalence of chronic kidney disease among the current Renal REGARDS participants may surprisingly be much less than is reported in the NHANES III samples of nondiabetics by Clase, Garg, and Kiberd [3] (Table 2). We used the MDRD equation [8] to estimate kidney function for the Renal REGARDS participants. Estimated GFR using the four-variable MDRD equation will be available for the entire REGARDS cohort, but for the analysis of Renal REGARDS, the six-variable MDRD equation [8] is being used because serum albumin and serum urea nitrogen, in addition to creatinine, are available. While considerable controversy exists about the most appropriate estimating equations for estimated GFR [3, 4], we have used the same estimating GFR equation as Clase, Garg, and Kiberd [3] for the comparisons of the data presented in Table 2. Formal, adjusted comparisons of the two populations will await the completion of recruitment for the REGARDS Study.

There are strengths to our study that should be noted. Most important, REGARDS is a unique sample of the United States population, with a recruitment strategy that emphasizes the population (blacks and Southeastern United States) at risk for stroke. Second, we limited our sample to individuals aged 45 years and older, the portion of the United States population most at risk of chronic kidney disease and ESRD. This allows us to examine patterns and risk factors for moderate to severe chronic kidney disease with sufficient numbers of cases to provide statistically stable estimates of effect. The addition of hemoglobin measurements, and albumin and serum urea nitrogen in the Renal REGARDS cohort, and the use of a single central laboratory for all analyses will permit more precise determinations of estimated GFR, and a prospective assessment of the independent risk of anemia for stroke, chronic kidney disease, and cardiovascular disease. As will be the case for most large epidemiologic efforts, a limitation of the REGARDS Study is that GFR must be estimated rather than directly measured. This is due to the expense and inherent difficulties in measuring GFR or collecting accurate creatinine clearances in a population of 30,000 participants. Furthermore, the single determination of serum creatinine and serum urea nitrogen supports a single estimate of the GFR, and does not formally fulfill the precise definition of chronic kidney disease, according to the KDOQI guidelines of the National Kidney Foundation [9]. If follow-up home visits and repeat blood samples become possible, then the associated risk factors for stroke, chronic kidney disease, and cardiovascular disease could be related to the proportion of the participants who showed changes in their kidney function over time.

CONCLUSION

We have described a large, unique cohort of participants who have been identified to be at relatively high risk for incident stroke, chronic kidney disease, and cardiovascular disease. In the participants who are balanced with respect to gender and white or black ethnicity, the prevalence of chronic kidney disease is higher in the higher age strata. Not surprisingly, the average hemoglobin is lower in the presence of chronic kidney disease, defined

as estimated GFR <60 mL/min/1.73 m^2. Whether or not there are associations between the prevalence of chronic kidney disease, anemia, and stroke, as suggested by the previous ARIC Study [2], are important public health questions that the REGARDS Study will specifically address.

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